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# PATENT SPECIFICATION

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COMPLETE SPECIFICATION

## Dentifrice Composition and method of making same

We, BRISTOL-MYERS COMPANY, a corporation organized under the laws of the State of Delaware, United States of America, of 630 Fifth Avenue, New York, State of New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to dentifrices, and more particularly to dentifrices in paste or powder form containing a water-soluble fluoride and a water-insoluble alkali-metal metaphosphate abrasive material.

It is generally accepted that dental caries result at least in part from the acids formed by microorganisms in the mouth in the course of their metabolism. These acids, when in contact with the teeth, attack the enamel of the teeth, dissolving the enamel, and result in tooth decay. A great deal of research effort has been devoted to finding methods and means for protecting the teeth from the attack of these acids. One of the proposals which has received considerable attention is the use of water-soluble fluorides, such a sodium fluoride or stannous fluoride as an active ingredient in a dentifrice as a means of retarding caries. The fluoride ion is believed to react with the hydroxyapatite which makes up dental enamel to form fluorapatite. The latter is believed to be less amenable to acid attack. Whatever the reason, many dental scientists feel that treatment of the teeth with a fluoride helps to protect the teeth from caries formation.

It has further been found that it is necessary to maintain the pH of a dentifrice system on the acid side and preferably, at pHs of 4.5 or 5.5 or below to obtain satisfactory fluoride uptake by dental enamel. However, the lower pHs are known to increase the solubility of dental enamel in said system. It has now been discovered that this solubility of dental enamel at lower pHs may be dramatically reduced by incorporating an insoluble alkali metal metaphosphate and particularly, insoluble-sodium metaphosphate (IMP) in the dentifrice system.

The insoluble alkali-metal metaphosphates and particularly insoluble-sodium metaphosphate have properties that make them very desirable as abrasives for use in dentifrice systems. In prior dentifrice systems in which they were incorporated, the art teaches the necessity of also incorporating therein sacrificial metal, e.g. calcium. This was thought necessary in order to prevent the uptake of calcium from dental enamel. However, use of sacrificial calcium is detrimental to a dentifrice system which also includes water-soluble fluorides. This is due to the fact that the calcium ion tends to react with fluoride ion in an aqueous system to form highly water-insoluble calcium fluorides which are not effective for the intended purpose of the fluorides. Moreover, the presence of calcium is believed to help nucleate crystallization on teeth in the formation of calculus.

It has now been found, in accordance with the present invention, that the tendency of insoluble-sodium metaphosphate in a dentifrice system to take up calcium can effectively be curtailed by maintaining the pH of the dentifrice system on the acid side and particularly, at pHs of 4.5 or 5.5 below. This makes it possible to eliminate the sacrificial metal like calcium utilized in prior art systems of this character and to avoid the danger of inactivating the fluoride ion in systems containing the water-insoluble fluorides. As used herein, calcium is considered sacrificial when it is present in a form such as to be capable of yielding 10 ppm of Ca ion in aqueous solution. Thus, extremely refractory Ca salts, incapable of providing sacrificial calcium ion, may also be present.

It is accordingly an object of the present invention to provide a fluoride containing dentifrice system which has a pH on the acid side and preferably, a pH of 4.5 or 5.5 or

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below so as to facilitate the uptake of fluoride by dental enamel and at the same time to reduce the tendency of such a system to dissolve dental enamel.

It is also an object of the present invention to provide a fluoride containing dentifrice system containing insoluble alkali-metal metaphosphate and particularly, insoluble-sodium metaphosphate without the need for incorporating therein sacrificial metal.

In accordance with the present invention there is provided a dentifrice comprising a substantially sacrificial-metal-ion-free dentifrice vehicle, an inorganic water-soluble fluoride capable of retarding caries, and insoluble alkali-metal metaphosphate abrasive, said dentifrice being buffered on the acid side at a pH, when the pH is measured in an aqueous medium, which can be tolerated by oral tissues with a buffer system selected from the group consisting of phosphate buffers, capable of adjusting pH to the acid side, and hydroxy carboxylates, said hydroxy carboxylates being utilized when said water-soluble fluoride tends to form insoluble salts with the phosphate buffer. As used herein, the term buffer includes any material which will serve to stabilize the pH of this system within the desired range.

The buffering agent employed can vary and will be dependent on the type of water-soluble fluoride that is incorporated in the system. Thus, for example, where the water-soluble fluoride is an alkali-metal fluoride, such as sodium fluoride, it is advantageous to use a water-soluble orthophosphate (including orthophosphoric acid) as the buffering agent. This buffer system is particularly preferred, since it further assists in the uptake of fluoride ion by the dental enamel and also assists in the remineralization of teeth.

Where the water-soluble fluoride tends to be unstable in the dentifrice system and to decompose to form insoluble-metal ion species, as in the case of stannous fluoride, or where they would form insoluble salts with the orthophosphate buffer, it is advantageous to select a buffer which will complex the unstable metal ion. Organic hydroxy carboxylates and particularly, aliphatic or aromatic hydroxy carboxylates capable of complexing the metal ion species are especially suitable for this purpose. As used herein, the term carboxylate is intended to cover the free acid and its corresponding salts.

As has been stated hereinabove, it is desirable that the pH of the dentifrice does not exceed about 5.5. There is no essential minimum pH value, and the pH of the dentifrice may be as low as the ability of the oral cavity of the user to withstand the acidity. The acidity which can be tolerated by the user depends somewhat upon the mode of application of the dentifrice and the frequency of its use. For example, a dentist would apply a dentifrice to his patient relatively infrequently and would carefully apply it directly to the teeth of the patient without more than superficially touching the mucous linings of the mouth of the patient. Under these circumstances the dentist may find it feasible to employ a dentifrice having a pH of as low as 2.5. For a general purpose commercial dentifrices which may be applied by the consumer as much as three times a day, it would probably not be desirable for the dentifrice to have a pH of below about 3.5. However, a pH of between 4 and 5 is preferred.

The water-soluble fluoride component of the dentifrices of the present invention may comprise any of the water-soluble fluorides suitable in dental hygiene. It may comprise hydrofluoric acid in aqueous solution, or an alkali-metal or ammonium salt, such as the fluoride salts of sodium, potassium, lithium or ammonium or a water-soluble fluoride of a transition metal, such as the salts of manganese and tin, i.e., stannous fluoride. For the purposes of this invention, sodium fluoride is preferred. The amount of water-soluble fluoride may vary considerably depending upon the frequency and mode of application. In general an amount of from about 0.05% to about 5% by weight of the total composition will usually suffice. The amount employed will preferably range between about 0.1% and 2% by weight. In accordance with accepted standards tooth pastes will preferably contain about 0.22% by weight of fluoride if the fluoride is sodium fluoride and 0.40% by weight of stannous fluoride.

The insoluble-alkali metal metaphosphate which is employed in accordance with this invention may serve as the abrasive and may constitute the sodium, potassium or ammonium insoluble metaphosphates. These insoluble metaphosphates are obtained by thermally decomposing the mono-sodium, potassium or ammonium phosphates. The resulting insoluble metaphosphates are frequently referred to as Maddrell's salts, and they are described by J. R. Van Wazer in "Phosphorus and Its Compounds," Vol. I, pages 665—678, Interscience Publishers (1958). Preferably, the abrasive or polishing agent of the dentifrice is made up solely of insoluble alkali-metal metaphosphate. However, the polishing agent may also consist of other noncalcium-containing abrasives together with the insoluble alkali-metal metaphosphate.

It is important that the dentifrice contains at least 5% by weight of its total composition of insoluble alkali-metal metaphosphate. In general, it is desirable that the dentifrice contain a total of about 40 to 70% by weight of abrasive or polishing agent when the dentifrice is a paste and above about 90% when the dentifrice is in the form of a powder. In accordance with the present invention the other noncalcium-containing polishing agent

which may be used together with the insoluble alkali-metal metaphosphate does not provide sacrificial calcium to the composition. Included among these noncalcium-containing polishing agents are aluminum oxide, titanium dioxide, ground pumice, powdered nylon, ground melamine-aldehyde resins, lactose, calcined aluminum silicate, and micro-crystalline cellulose. Preferably, not more than about 40% of the total polishing agent or abrasive is an agent other than an insoluble alkali-metal metaphosphate.

The orthophosphate buffer need only be water-soluble and may be employed in almost any desirable amount. One form of the orthophosphate is phosphoric acid *per se* and it is highly feasible to employ this compound as a means of acidifying the dentifrice and reducing the pH to below about 5.5. It is preferred however to also employ an alkali metal orthophosphate. This class is intended to include the ammonium salt and salts of organic bases as well as salts of alkali-metals. Thus, sodium, potassium, ammonium, monoethanolamine salts may be employed in the mono-, di- or tribasic forms obtainable with phosphoric acid. While there is no real limitation on the amounts employed, so long as they do not adversely interfere with the pH of the dentifrice, it is generally feasible to employ from 0.25% up to 10% by weight of the total composition with the maximum preferably not exceeding about 5%. For most purposes 2% by weight of orthophosphate provides highly suitable results.

As mentioned above, in some instances organic hydroxy carboxylates and particularly, the aliphatic or aromatic hydroxy carboxylates are the buffering agents of choice. These may be mono-, di-, tri- or polyhydroxy carboxylic acids or their salts. Although these buffers are described as acids or salts, since they are added to the composition as such, it is to be understood that under the conditions obtaining in the dentifrice system, they exist as a buffer system which includes both the acid and the salt. Among the hydroxy carboxylates which are useful for the present purposes may be mentioned: sodium malate, malic acid, citric acid, tartaric acid, tartronic acid and salicylic acid. The organic hydroxy carboxylate is present in amounts, preferably, ranging from 0.05 to 5% by weight of the dentifrice composition.

In addition to the foregoing, the dentifrice can contain as optional ingredients surface tension depressants if they are reasonably stable within the pH range of the dentifrice. Examples include, but are not limited to, water-soluble alkyl and alkyl ether sulfates, and sulfonates having alkyl groups containing from 8 to 18 carbon atoms, such as sodium lauryl sulfate and sodium lauryl ether sulfate, salts of fatty acid esters of isethionic acid, such as sodium lauryl isethionate, or sodium mixed alkyl isethionates, water-soluble salts of saturated higher aliphatic acyl amides of saturated lower aliphatic monoaminocarboxylic acids such as those having from 10 to 20 carbon atoms in the long chain fatty acyl radical and from 2 to 6 carbon atoms in the amino acid radical, water-soluble salts of sulfonated mono glycerides of fatty acids and water-soluble salts of sulfonated hydrocarbons having from 8 to 20 carbon atoms, such as sulfonated decanes, dodecanes and octadecanes. Particularly good results are obtained with "Tweens," such as "Tween" 60 which is the polyoxyethylene derivative of sorbitan mono stearate. The word "Tween" is a registered Trade Mark.

Mixtures of two or more of the surface tension depressants can be used.

Other optional conventional components of a dentifrice which may be present include flavoring materials, such as the flavoring oils (e.g. peppermint oil); sweeteners, such as sucrose, glucose, saccharin and sodium cyclamate, and harmless coloring materials, in proportion to give any desired taste or flavor or other effect.

In a preferred embodiment of the invention, the dentifrice is in the form of a paste, and in this event it will contain a carrier and softener and a binder in amounts to give the dentifrice a smooth texture and a good flowability. Glycerin, propylene glycol and sorbitol are preferred humectants, carriers and softeners, but syrup, glucose and invert sugars and honey can also be employed. These may be used singly or in combinations. As binders there can be employed natural or synthetic gums or bentonite or montmorillonite clays, such as carboxymethylcellulose, gum tragacanth, sodium alginate, Irish moss, gum acacia, pectin, colloidal hydrated magnesium aluminum silicate, sodium bentonite, polypropylene glycol esters of alginic acid and combinations thereof. Those skilled in the dentifrice art will know of other carriers, softeners and binders which may also be used. The pastes may be either of the aqueous type, containing substantial amounts of water (above 18% by weight), or of the relatively anhydrous type, containing less than 5% by weight water. Formulations are given below for both types.

In addition to pastes, the dentifrices of the invention may be in the form of powders. The main difference between a paste and powder is that the latter contains little or no water and usually no binder or softener.

As noted above, the addition of insoluble-sodium metaphosphate reduces the solubility of human dental enamel in acid solution. This is clearly illustrated in the data given in Table I below. In column 2 the percent reduction of the solubility of human dental enamel in an acid solution having the pH indicated and containing insoluble-sodium metaphosphate

(I.M.P.) when compared with an acid solution of the same pH without the addition of I.M.P. is given. Column 3 gives similar data for equivalent solutions containing both the I.M.P. and the orthophosphate buffer.

TABLE I

| Test pH | Percent Reduction | |
|---|---|---|
| | I.M.P. alone | I.M.P. + $PO_4$ (5%) |
| 3.60 | −20% | −20% |
| 3.75 | −42 | −42 |
| 4.00 | −66 | −66 |
| 4.25 | −80 | −80 |
| 4.50 | −84 | −86 |
| 4.75 | −83 | −85 |
| 5.00 | −40 | −66 |

The dentifrice compositions of the present invention have been tested clinically in caries studies involving 1952 subjects. Table II summarizes the results of a six-month study.

The figures expressed below represent the differences in new decayed and filled surfaces between the groups using commercially available sodium fluoride and stannous fluoride formulae as well as the groups using examples of the IMP formulae of the present invention. The frame of reference in this instance is a conventional, commercially available, non-fluoride formula.

TABLE II

| | No. of Subjects | % Reduction |
|---|---|---|
| Stannous fluoride — calcium pyrophosphate system | 395 | 3.70 |
| Sodium fluoride — dicalcium phosphate system | 414 | 2.47 |
| Sodium fluoride — insoluble-sodium metaphosphate system | 331 | 47.53 |
| Stannous fluoride — insoluble-sodium metaphosphate system | 432 | 17.9 |
| Control | 380 | — |

As may be seen by a review of the data, the present stannous fluoride IMP formula offered greater protection than the stannous fluoride formula containing calcium pyrophosphate as the major abrasive ingredient. It may also be noted that the sodium fluoride IMP formula of this invention was superior in performance to the sodium fluoride product containing dicalcium phosphate as its abrasive agent.

The following are general formulations of tooth pastes and powders of the type contemplated according to the present invention (parts are expressed in terms of parts by weight):

Aqueous Tooth Paste

| | Parts by Weight |
|---|---|
| Water-soluble fluoride | 0.05 to 5.0 |
| Water | 15 to 25 |
| Binder | 0.8 to 1.2 |
| Polishing agent | 40 to 50 |
| Softener or humectant | 20 to 25 |
| Detergent | 0 to 2 |
| Sweetener | 0.1 to 0.2 |
| Flavoring oils | 0.9 to 1.2 |
| Buffering Agent | Sufficient amount to give the composition a pH of no greater than 5.5 |

Substantially Anhydrous Tooth Paste

| | Parts by Weight |
|---|---|
| Water-soluble fluoride | 0.05 to 5.0 |
| Water | 0 to 4.5 |
| Binder | 0.3 to 1.2 |
| Polishing agent | 45 to 70 |
| Humectant | 25 to 45 |
| Detergent | 0 to 2 |
| Sweetener | 0.03 to 0.10 |
| Flavoring oils | 0.9 to 1.2 |
| Buffering Agent | Sufficient amount to give the composition a pH of no greater than 5.5 when the composition is mixed with water |

Powder

| | Parts by Weight |
|---|---|
| Water-soluble fluoride | 0.05 to 5.0 |
| Polishing agent | 90 to 98 |
| Detergent | 1 to 3 |
| Flavoring oils | 0.85 to 1.2 |
| Sweetener | 0.1 to 0.2 |
| Buffering Agent | Sufficient amount to give the composition a pH of no greater than 5.5 when the composition is mixed with water |

In order more clearly to disclose the nature of the present invention, specific examples illustrating the preparation of typical dentifrices will hereinafter be described. Unless otherwise stated, quantities of materials are referred to in terms of parts by weight. The materials are mixed together in accordance with the standard practice in the dentifrice art.

The term "insoluble-sodium metaphosphate" as used herein refers to the so-called high-temperature variety of Maddrell's salt which is designated symbolically in the art as $NaPO_3$—II. This is readily made in quite pure form by heating monosodium orthophosphate at 400°C in the presence of steam. (See J. R. Van Wazer citation noted above).

EXAMPLE 1

The following is an example of a tooth paste formulation:

| Ingredient | Parts by Weight |
|---|---|
| sodium fluoride | 0.22 |
| water (deionized) | 18.33 |
| magnesium aluminium silicate (Veegum) | 1.00 |
| insoluble-sodium metaphosphate | 48.00 |
| humectant (mixture of glycerin and sorbitol [1:3 by weight]) | 22.50 |
| soluble saccharin | 0.15 |
| carboxymethylcellulose | 1.20 |
| sodium lauryl sulfate | 1.70 |
| monosodium orthophosphate | 1.00 |
| phosphoric acid (10% by weight aqueous solution) | 5.00 |
| flavoring oils | 0.90 |
| | 100.00 |

(The pH of this dentifrice was about 4.5)

EXAMPLE 2

The following is an example of a tooth paste formulation:

| Ingredient | Parts by Weight |
|---|---|
| hydrogen fluoride | 0.15 |
| water (deionized) | 18.40 |
| magnesium aluminium silicate (Veegum) | 1.00 |
| insoluble-sodium metaphosphate | 48.00 |
| glycerin | 22.50 |
| soluble saccharin | 0.15 |
| carboxymethylcellulose | 1.20 |
| sodium lauryl sulfate | 1.70 |
| monosodium orthophosphate | 1.00 |
| phosphoric acid (10% by weight aqueous solution) | 5.00 |
| flavoring oils | 0.90 |
| | 100.00 |

(The pH of this dentifrice was about 4.0)

EXAMPLE 3

The following is an example of a tooth paste formulation:

| Ingredient | Parts by Weight |
|---|---|
| potassium fluoride | .30 |
| water (deionized) | 18.25 |
| magnesium aluminium silicate (Veegum) | 1.00 |
| insoluble-sodium metaphosphate | 28.00 |
| lactose | 20.00 |
| humectant (mixture of glycerin and sorbitol [1:3 by weight]) | 22.50 |
| soluble saccharin | 0.15 |
| carboxymethylcellulose | 1.20 |
| sodium lauryl sarcosinate | 1.70 |
| monosodium orthophosphate | 1.00 |
| phosphoric acid (10% by weight aqueous solution) | 5.00 |
| flavoring oils | 0.90 |
| | 100.00 |

(The pH of this dentifrice was about 4.5)

EXAMPLE 4

The following is an example of a tooth paste formulation:

| Ingredient | Parts by Weight |
|---|---|
| ammonium fluoride | .19 |
| water (deionized) | 18.36 |
| magnesium aluminium silicate | 1.00 |
| insoluble-sodium metaphosphate | 28.00 |
| lactose | 10.00 |
| powdered nylon | 10.00 |
| humectant (mixture of glycerin and sorbitol [1:3 by weight]) | 22.50 |
| soluble saccharin | 0.15 |
| carboxymethylcellulose | 1.20 |
| sodium lauryl sulfate | 1.70 |
| monosodium orthophosphate | 1.00 |
| phosphoric acid (10% by weight aqueous solution) | 5.00 |
| flavoring oils | 0.90 |
| | 100.00 |

(The pH of this dentifrice was about 4.5)

EXAMPLE 5

The following is an example of a tooth powder formulation:

| Ingredient | Parts by Weight |
|---|---|
| sodium fluoride | 0.2 |
| insoluble-sodium metaphosphate | 84.0 |
| monosodium orthophosphate | 2.5 |
| calcined aluminium silicate ("Kaopolite") | 5.0 |
| lactose | 5.0 |
| sodium lauryl sulfate | 2.0 |
| soluble saccharin | 0.2 |
| flavoring oils | 1.1 |
| | 100.00 |

EXAMPLE 6

| Ingredient | Percent by Weight |
|---|---|
| water (Deionized) | 18.23 |
| sweetener | 0.15 |
| sodium malate | 0.42 |
| lactose | 7.00 |
| stannous fluoride | 0.40 |
| humectant (mixture of glycerin and sorbitol [1:3 by weight]) | 22.35 |
| insoluble-sodium metaphosphate | 48.00 |
| flavor | 0.85 |
| sodium alginate | 1.00 |
| sodium lauryl sulfate | 1.60 |
| | 100.00 |

EXAMPLE 7

| Ingredient | Percent by Weight |
|---|---|
| water (deionized) | 22.88 |
| phosphoric acid | 0.50 |
| monosodium phosphate | 1.00 |
| sweetener | 0.15 |
| sodium fluoride | 0.22 |
| humectant (mixture of glycerin and sorbitol [1:3 by weight)] | 22.50 |
| insoluble-sodium metaphosphate | 48.00 |
| flavor | 0.85 |
| carboxymethylcellulose | 1.20 |
| magnesium aluminium silicate (Veegum) | 1.00 |
| sodium lauryl sulfate | 1.70 |
| | 100.00 |

WHAT WE CLAIM IS:—

1. A dentifrice comprising a substantially sacrificial-metal-ion-free dentifrice vehicle, an inorganic water-soluble fluoride capable of retarding caries, and insoluble alkali-metal metaphosphate abrasive, said dentifrice being buffered on the acid side at a pH, when the pH is measured in an aqueous medium, which can be tolerated by oral tissues with a buffer system selected from the group consisting of phosphate buffers, capable of adjusting pH to the acid side, and hydroxy carboxylates, said hydroxy carboxylates being utilized when said water-soluble fluoride tends to form insoluble salts with the phosphate buffer.

2. A composition according to claim 1, wherein the pH is not greater than about 5.5.

3. A composition according to claim 2, wherein the pH is between 3.5 and 5.5, and preferably between 4 and 5.

4. A composition according to any one of the preceding claims, wherein the water-soluble fluoride is hydrogen fluoride, an alkali-metal fluoride, ammonium fluoride, or a transition metal fluoride.

5. A composition according to claim 4, wherein the water-soluble fluoride is sodium fluoride.

6. A composition according to any one of the preceding claims, wherein the insoluble alkali-metal metaphosphate is insoluble-sodium metaphosphate.

7. A composition according to any one of the preceding claims, wherein the pH is buffered on the acid side with a water-soluble alkali-metal orthophosphate, preferably constituting .25—10% by weight of the composition.

8. A composition according to any one of claims 1 to 6, wherein the pH is buffered on the acid side with a hydroxy carboxylate, prefereably constituting .05—5% by weight of the composition.

9. A composition according to claim 8, wherein the hydroxy carboxylate is an aliphatic hydroxy carboxylate.

10. A composition according to any one of the preceding claims, wherein up to about 40% by weight of the insoluble alkali-metal metaphosphate abrasive is replaced by a non-sacrificial metal-ion-containing abrasive.

11. A composition according to any one of the preceding claims, comprising a substantially calcium-ion-free dentifrice vehicle, from about 0.05 to about 5% by weight of a water-soluble fluoride and at least 5% by weight of an insoluble alkali-metal metaphosphate abrasive, said dentifrice having a pH of not greater than about 5.5.

12. A dentifrice composition comprising a substantially sacrificial metal-ion-free vehicle, from about .05 to about 5% by weight sodium fluoride, at least 5% by weight of insoluble-sodium metaphosphate abrasive to which is added from .25 to 10% by weight of an alkali metal orthophosphate to buffer the composition at a pH not greater than about 5.5.

13. A dentifrice composition comprising a substantially sacrificial metal-ion-free vehicle, from about .05% to 5% by weight of stannous fluoride, at least 5% by weight of insoluble-sodium metaphosphate, to which is added from .05% to 5% by weight of a hydroxy carboxylate preferably an aliphatic hydroxy carboxylate to buffer the composition at a pH of not greater than about 5.5.

14. A composition according to any one of the preceding claims, wherein the composition contains at least about 40% by weight of substantially sacrificial metal-ion-free abrasive, at least 60% of which is an insoluble alkali-metal metaphosphate.

15. A composition according to claim 14 in which the insoluble alkali-metal metaphosphate is insoluble sodium metaphosphate.

16. A dentifrice according to claims 1 to 6, 8 to 11 and 13 to 15 wherein said hydroxy carboxylate is sodium malate.

17. A dentifrice according to claim 16 wherein said water-soluble fluoride is stannous fluoride.

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